

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
US Department of Commerce  
United States Patent and Trademark  
Office, PCT  
2011 South Clark Place Room  
CP2/5C24  
Arlington, VA 22202  
ETATS-UNIS D'AMERIQUE  
in its capacity as elected Office

Date of mailing (day/month/year)  
19 June 2001 (19.06.01)

International application No.  
PCT/US00/24213

Applicant's or agent's file reference  
UMDNJ 99-33

International filing date (day/month/year)  
01 September 2000 (01.09.00)

Priority date (day/month/year)  
02 September 1999 (02.09.99)

## Applicant

PESTKA, Sidney et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
24 March 2001 (24.03.01)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Odile ALIU

Telephone No.: (41-22) 338.83.38

REC'D 16 APR 2002

PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

10/088143

Applicant's or agent's file reference UMDNJ 99-33	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/24213	International filing date (day/month/year) 01 SEPTEMBER 2000	Priority date (day/month/year) 02 SEPTEMBER 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): C07H 21/02, 21/04 and US Cl.: 536/23.1		
Applicant UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  26 MARCH 2001	Date of completion of this report  01 MARCH 2002
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Jay-Bridges</i> SHANON FOLEY
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24213

## I. Basis of the report

1. With regard to the **elements** of the international application:\*☒ the international application as originally filed☒ the description:

pages 1-38 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the claims:

pages 39-41 , as originally filed  
pages NONE , as amended (together with any statement) under Article 19  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the drawings:

pages 1-9 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

☒ the sequence listing part of the description:

pages 1-6 , as originally filed  
pages NONE , filed with the demand  
pages NONE , filed with the letter of \_\_\_\_\_

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☒ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE  
☒ the claims, Nos. NONE  
☒ the drawings, sheets/fig NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\*Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/24213

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. statement**

Novelty (N)	Claims <u>3 and 6-11</u>	YES
	Claims <u>1, 2, 4, 5, 12, 13</u>	NO
Inventive Step (IS)	Claims <u>3 and 9-11</u>	YES
	Claims <u>1, 2, 4, 5-8, 12, 13</u>	NO
Industrial Applicability (IA)	Claims <u>1-13</u>	YES
	Claims <u>NONE</u>	NO

**2. citations and explanations (Rule 70.7)**

Claims 1, 2, 4, and 5 lack novelty under PCT Article 33(2) as being anticipated by Razzaque et al.

The claims are drawn to a nucleic acid molecule which encodes a polypeptide having a sequence variant of SEQ ID NO. 2 comprising a Thr residue inserted after Ala at position 26 in a vector.

Razzaque et al. teaches a cloned fragment of the CMV genome, termed the EM plasmid. This fragment comprises the genomic region recited in claim 1, thereby clearly anticipating claims 1 and 2. Razzaque et al. does not teach the full length sequence of the EM plasmid; however, the portion of the sequence disclosed in figure 2 includes nearly all of SEQ ID NO: 1. Since the EM plasmid extends well beyond the sequence presented in Figure 1, the EM plasmid inherently comprises SEQ ID NO: 1, and inherently encodes the polypeptide recited in claim 4. Therefore, the teachings of Razzaque et al. anticipate claims 1, 2, 4

Claims 12 and 13 lack novelty under PCT Article 33(2) as being anticipated by Muralidhar et al.

The claims are drawn to a method and a kit for detecting cmv-IL10 with antibodies that are specific for a cmvIL-10 protein.

Muralidhar et al. teaches a 79 amino acid open reading frame of the UL111a gene encoding the mtrII protein, which encompasses the cmv-IL10 gene. Since these genes overlap, an epitope encompassed by both genes would be inherent.

Muralidhar et al. teaches immunohistochemistry of noninfected and HCMV-infected cells and identifies the mtrII oncoprotein was stained with Ab-471 and detected with anti-rabbit IgG conjugated to horseradish peroxidase, see "Immunofluorescence and immunohistochemistry" on page 8693 and therefore anticipates a method for detecting an epitope of cmvIL-10 in an infected sample with ingredients claimed in the kit.

Claims 6-8 lack an inventive step under PCT Article 33(3) as being obvious over Razzaque et al. Razzaque et al. does not teach an isolated cmvIL-10 protein. However, the reference teaches a plasmid encoding the nucleotide sequences that are capable of expressing the cmvIL-10 protein, see the text cited above. Therefore, it would be obvious for the skilled artisan to use the plasmid that expresses the plasmid taught by Razzaque et al. in order to purify and isolate the protein.

Claim 3 meets the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest plasmid pEF-SPFL-cmv.

Claims 9-11 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest a method of treating a condition by administering cmvIL-10 or a component that is capable of sequestering cmvIL-10 as a method of treating a pathological condition caused by CMV.

(Continued on Supplemental Sheet.)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because: Claims 9-11 are drawn to a method of treatment by administering cmvIL-10 to treat a disease that would respond to treatment with cmvIL-10 and a substance that is capable of sequestering cmvIL-10. The description fails to teach treatment of any disease by administering cmvIL-10 or a composition that disrupts cmvIL-10 function. In addition, the description fails to provide evidence that inhibition of IL-10 would have an impact on the CMV life cycle in order to treat any disease associated with CMV infection. There is no teaching in the prior art of cmvIL-10, or the role it has in disease. Therefore, it is uncertain how one skilled in the art would administer an effective amount of cmvIL-10, or what effect it would have on any disease. Redpath et al. teaches that late expression of IL-10 by the immune system is normal in response to a pathogen. However, CMV infection causes premature and transient activation of host IL-10, which interferes with natural host defense by reducing the expression of MHC class II on the surface of cells. Although the reference teaches that inhibition of MHC class II expression was not observed in the presence of neutralizing antibodies to IL-10, there is no teaching that antibody interference with IL-10 had an impact on CMV infection or CMV life cycle. Therefore, due to the nature of the claims, which is drawn to treat any disease with cmvIL-10, or CMV-related disease with an unknown substance that is not known to have a mechanism to interfere with CMV life cycle, or improve immune response against disease, and the state of the art at the time the invention was made, it is determined that undue experimentation would be required of the skilled artisan to make and/or practice the claimed invention.

Claim 9-11 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):**

Database TrEMBLrel, Accession number Q89858, RAZZAQUE et al. Hypothetical 8.7 KDA Protein. 01 November 1996. Sequence alignment.

MURALIDHAR et al. Human cytomegalovirus mtrII oncoprotein binds to p53 and down-regulates p53-activated transcription. Journal of Virology. December 1996, Vol. 70, No. 2, pages 8691-8700.

REDPATH et al. Murine cytomegalovirus infection down-regulates MHC class II expression on macrophages by induction of IL-10. Journal of Immunology. 1 June 1999, Vol. 162, No. 11, pages 6701-6707, see the abstract.

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY.

## PCT

### NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To: JANET E. REED CENTRE SQUARE WEST 1500 MARKET STREET 38TH FLOOR PHILADELPHIA PA 19102
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Date of Mailing (day/month/year)	12 APR 2002
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Applicant's or agent's file reference UMDNJ 99-33		IMPORTANT NOTIFICATION	
International application No. PCT/US00/24213	International filing date (day/month/year) 01 SEPTEMBER 2000	Priority Date (day/month/year) 02 SEPTEMBER 1999	
Applicant UNIVERSITY OF MEDICINE AND DENTISTRY OF NEW JERSEY			

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer SHANON FOLEY  Telephone No. (703) 308-0196
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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/24213

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : C07H 21/02, 21/04

US CL : 536/23.1

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 536/23.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ----- Y	RAZZAQUE. A. Localization and DNA sequence analysis of the transfo rming domain (mtrII) of human cytomegalovirus. Proc. Natl. Acad. Sci. August 1988, Vol. 85, pages 5709-5713 see entire document.	6-8 ----- 9-13

☐

Further documents are listed in the continuation of Box C.

☐

See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*A* document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*E* earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	* & * document member of the same patent family
*O* document referring to an oral disclosure, use, exhibition or other means	
*P* document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

20 OCTOBER 2000

Date of mailing of the international search report

22 JAN 2001

Name and mailing address of the ISA/US  
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BRETT L NELSON

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TERRY J. DEY  
PARALEGAL SPECIALIST  
TECHNOLOGY CENTER 1600

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/24213

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

WEST, DIALOG, MEDLINE, SCISEARCH, BIOSIS, EMBASE

search terms: cytomegalovirus, IL-10, CMV, DNA, protein, amino acid, polypeptide, antibodies, diagnostic, pharmaceutical, treatment